



Historical paper

## 20th Anniversary Meeting of the Meryon Society Worcester College, Oxford

Alan E.H. Emery<sup>a</sup>, Marcia Emery<sup>b</sup>, Michael Swash<sup>c,d</sup>, Jacqueline Mikol<sup>e</sup>, Olivier Walusinski<sup>e</sup>,  
Hans H. Goebel<sup>f,\*</sup>

<sup>a</sup> Green Templeton College, University of Oxford, UK

<sup>b</sup> Templeton College, University of Oxford, UK

<sup>c</sup> Barts and the London School of Medicine, QMUL, London, UK

<sup>d</sup> Institute of Neuroscience, University of Lisbon, Portugal  
<sup>e</sup> Paris

<sup>f</sup> Institute of Neuropathology, Charité, Berlin, Germany

### Introduction

Among the muscular dystrophies, Duchenne Muscular Dystrophy is the most prominent form having given rise to the eponym of its gene *DMD* (i.e. *Duchenne Muscular Dystrophy*), the probably earliest identified myonological entity and the first description of which is contested as in no other muscular dystrophy or neuromuscular disease. This contest emulates the 100-year war between France and Britain (“The honor of this discovery totally belongs to France”) (Duchenne 1868) (but, perhaps, Duchenne might not have been wrong after all because Meryon came from a French Huguenot family and primarily studied medicine in Paris), essay by Mikol and Walusinski below). This smoldering controversy has recently been rekindled by the historical research of Marcia and Alan Emery (the latter one being the sole medical person whose name has prompted geneticists to name a protein, emerin, after him – and its gene *EMD*, i.e. *Emery Muscular Dystrophy*) on Edward Meryon (see below), the British contestant in this eponymic struggle, finally having resulted in the monograph “The History of a Genetic Disease – Duchenne Muscular Dystrophy or Meryon’s Disease” and the foundation of the Meryon Society twenty years ago.

As this year, 2016, features the 20th Anniversary of the Meryon Society which holds annual meetings at and in conjunction with the annual Muscle Symposium in Oxford/UK with a Meryon Society Lecture as its central event published in “Neuromuscular Disorders”, a special section commemorating Edward Meryon’s seminal paper (Alan Emery), Edward Meryon’s life and the foundation of the Meryon Society

(Marcia Emery), and three small essays on the awareness of Meryon’s publication in Britain (Michael Swash), France (Jacqueline Mikol and Olivier Walusinski), and Germany (Hans H. Goebel) were added to the programme and will compose this short historical note.

### Edward Meryon: The Story of Muscular Dystrophy

Alan E.H. Emery, Green Templeton College, University of Oxford, Email: [alan.emery@gtc.ox.ac.uk](mailto:alan.emery@gtc.ox.ac.uk)

Meryon was the first clinical scientist to take a disease and describe it in detail clinically, to consider the inheritance, to study the pathology and to consider the aetiology. His first paper on the disease, published in 1852, was only 11 pages in length, and preceded the publications of Duchenne by 10 years.

His conclusions were based on six families, in five of which (7 sibships) only boys were affected. He concluded that there was a predilection for males, the disease was familial (brothers inherited, through their mothers), affected primarily muscle, the nervous system was found to be normal, and histologically the ‘sarcolemma. . .broken down and destroyed’.

### Familial Studies

He studied six families in which there were 18 affected males. Interestingly in one family he noted that a father only had an affected son by his second wife, and concluded that it was therefore passed through the maternal line.

### Muscle Histology

He carefully studied the muscle tissue in affected boys and concluded that the fibres were completely destroyed, due to breakdown of the sarcolemma.

\* Corresponding author for this series of short items constituting this anniversary report: Department of Neuropathology, Charité – Universitätsmedizin Berlin, Campus Charité Mitte, Charitéplatz 1 | Virchowweg 15, D-10117 Berlin, Germany. Fax: 0049-30-450-536-940.

E-mail address: [hans-hilmar.goebel@charite.de](mailto:hans-hilmar.goebel@charite.de) (H.H. Goebel).

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## Central Nervous System

In one case of a boy who died, he studied the spinal cord and concluded that there was no evidence of disease of the nervous system. When he compared the spinal cord of one of his patients with the spinal cord of a perfectly normal boy who died following an accident, he found there was no difference.

## Meryon's Conclusions

1. It was familial, only affected boys and was transmitted through females.
2. It was essentially a disease of muscle, the spinal cord being normal.
3. The significant pathology was a disruption of the sarcolemma.

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## Edward Meryon: His life and the establishment of the Meryon Society

Marcia Emery, Templeton College, University of Oxford,  
Email: [alan.emery@gtc.ox.ac.uk](mailto:alan.emery@gtc.ox.ac.uk)

Marcia Emery presented an illustrated talk on Edward Meryon's life and background, and the establishment of a Society in his name. The exact date of his birth is unknown but he was baptised in Rye, Sussex on December 10th 1807. His mother was a Jane Gatland (or Gateland), a seamstress aged 20, and his father was John Meryon (1776–1857) of Huguenot stock. His father never married his mother though he provided financial support.

It seems that Edward's early life was probably influenced by his uncle Charles Lewis Meryon MD FRCP (1783–1877), a physician and traveller. The details of Edward's early education are not clear but he states that in 1829 he studied medicine at the Hôtel Dieu and L'Ecole de Médecine in Paris (was there an opportunity to meet Duchenne?) and in the same year he registered as a medical student at University College in London. He was a brilliant student, collecting many prizes and medals.

He subsequently became a Member of the Royal College of Surgeons in 1831, later a Bachelor and subsequently Doctor of Medicine of the University of London, and was elected a Fellow of the Royal College of Physicians.

In February 1833 he married Catherine Baily of Falkingham, by whom he had four daughters and a son, John Edward, through whom the name Meryon has been passed down to the present generation.

Apart from a period as lecturer in Comparative Anatomy at St. Thomas's Hospital Medical School, most of his life was spent as a practising physician in London. He was a member of several illustrious bodies including the Athenaeum, the Royal Institution, the Geological Society and the Ethnological Society and was elected a Fellow of the Royal Medical & Chirurgical Society in 1846 where, five years later in 1851, he delivered his seminal paper "On Granular and Fatty Degeneration of the Voluntary Muscles" (*Med Chirurg Trans*, 1852, 35: 73–84). In 1868 he was appointed physician to what subsequently became the Maida Vale Hospital for Nervous Diseases.

In his later years he became Vice President of the Royal Medical & Chirurgical Society as well as Council Member of the Royal College of Physicians. He was clearly a distinguished and respected member of the medical community at the time. He died suddenly at home on Monday November 8th 1880 aged 73 and he is buried in Brompton Cemetery, London.

With all the research done on the life and work of Meryon, resulting in the publication of our book, *History of a Genetic Disease: Duchenne Muscular Dystrophy or Meryon's Disease* (2nd ed., Oxford university Press, 2011) it seemed that the next step would be to establish a society in his name, to continue to explore the historical work of Meryon and others in the field of neuromuscular diseases. The first meeting of the Society was held 20 years ago at the Royal Society of Medicine in London in September 1996. The aims of the Society were discussed followed by an illustrated talk on Edward Meryon's life and background given by myself. A descendent of Meryon's, Commander Peter Louis Meryon RN (retired) came to this meeting, bringing with him photographs and much information, which was helpful in filling in many details previously unknown about the family. The meeting was followed by a meal, but it was realised after this meeting that it would be financially impossible to continue the Society with such a small membership. However, the continued existence of the Society was enabled by the generosity of the late Dr. Christopher Fursdon Davis and the Oxford Muscle group, who arranged for the fledgling Meryon Society to hold its meeting along with theirs, and present a lecture during the Oxford Muscle Meeting's annual gathering. So the Meryon Society held its next meeting at the 1998 Oxford Muscle Symposium and has continued ever since, presenting an annual lecture to increase awareness of the historical background to Meryon and many other figures in the field of neuromuscular diseases.

Thanks to the efforts of the Meryon Society, a plaque was placed on the site of Meryon's former home on Clarges Street

in Piccadilly by the City of Westminster Council. And an entry under Meryon's name has been placed in the *Oxford Dictionary of National Biography* (2004) so that he will be credited in posterity for his achievements.

### Impact of Meryon's description of severe muscular dystrophy in Britain

Michael Swash, Barts and the London School of Medicine, QMUL, London; and Institute of Neuroscience, University of Lisbon, Portugal. Email: [mshwash@btinternet.com](mailto:mshwash@btinternet.com)

Recognition of pseudohypertrophic muscular dystrophy is generally ascribed to the work of Duchenne, whose description of the clinical and pathological features of the disease in 1861 and 1868<sup>1</sup>, its inheritance in the female line and presentation in young boys set the scene for further studies in subsequent years. However, Duchenne was not the first to recognise the disease. Gowers<sup>2</sup>, in his *Manual of Diseases of the Nervous System*, first published in 1893, wrote that '*Isolated cases, which can now be recognised as examples of this disease, were recorded in England in 1830 (Sir Charles Bell) and in 1847 (Partridge), and in Italy in 1838. A series of cases was described by Meryon in 1852, and Oppenheim in 1855, but enlargement of the muscles was not conspicuous in these*' (vol 1, page 506).

Gowers adds a footnote to this historical comment stating that Meryon's<sup>3</sup> cases '*certainly belonged to this variety*' and cites as conclusive proof his own clinical observations of '*collaterals other which have come under the writer's observation in near and distant members of the same family*'. He had discussed these issues in his *Lecture on Pseudohypertrophic Muscular Dystrophy*<sup>4</sup>, published in 1879, based on a series of lectures that had appeared in the same year in *The Lancet*. In this *Lecture* Gowers refers at some length to various early descriptions, including those of Meryon. It is clear that he was familiar with Meryon's work. Gowers, writing from the perspective of 1893, commented that Meryon had regarded the disease as '*identical with progressive muscular atrophy (Cruveilhier's atrophy)*', a disorder subsequently recognised as of neurogenic aetiology<sup>2</sup>. He noted that '*Dr Meryon only alluded incidentally to the feature, the enlargement of the muscles, which was seized upon as the most salient characteristic of the disease by the distinguished French physician, Duchenne, in an original description published in 1861*'. Gowers himself noted that enlargement of muscles was variable in extent and localisation, a circumstance that might account for '*the fact that it received little notice from Dr Meryon*'. Gowers<sup>4</sup> reviewed 220 published cases, 30 of whom were women. He noted that careful enquiry was required to uncover the proper familial incidence. He commented on Meryon's observation of a family in which three sisters had sons affected by the disease as correctly indicating female transmission. Importantly he concurred with Meryon's assertion concerning the absence of '*fibrillary twitching*' of muscles, thus distinguishing this primary muscle disease from amyotrophic lateral sclerosis. However, the continuing uncertainty about the clinical limits of pseudohypertrophic

muscular dystrophy at that time was attested by Gowers' discussion of Meryon's comment that the father of one of his cases was well-known to be weak, had difficulty getting up onto his horse, or onto the box of his carriage and could not jump over a ditch, and that his maternal uncle was similarly weak.<sup>4</sup> Finally, Gowers credits Meryon's description of the lack of relevant spinal pathology by discussing his own confirmatory pathological observations made jointly with Dr Lockhart Clarke, the foremost British expert on the pathology of the nervous system of that era.

Clearly, Gowers regarded Meryon's work as both original and important. However, Kinnier Wilson<sup>5</sup>, in his textbook of *Neurology* published in 1940, refers almost entirely to early twentieth century literature in his somewhat brief discussion of the primary muscle diseases. Walton and Nattrass<sup>6</sup> in their seminal re-classification of these disorders stated that '*Granular degeneration of the voluntary muscles in 4 brothers was described by Meryon in 1852 and it gradually became clear that cases of this type were clinically and pathologically distinct from another group of patients in whom muscular atrophy was secondary to changes in the grey matter of the spinal cord and in whom the disease was not usually familial*' – referring to amyotrophic lateral sclerosis, the spinal muscular atrophies and poliomyelitis.

Emery and Emery<sup>7</sup> have extensively researched Meryon's life and published work for their book on the history of Duchenne's, or perhaps Meryon's, muscular dystrophy. They point out that Meryon was a leader in the development of ideas on the cause(s) of progressive paralysis of muscles, especially with regard to early ideas on primary disease of muscle, as shown by his post mortem studies of muscle and spinal cord in an affected boy. Adams, Denny-Brown and Pearson<sup>8</sup> had earlier come to similar conclusions in their book on *Diseases of Muscle* published in 1953 (page 240) in which they stated '*Meryon therefore first established in 1864. . .an idiopathic disease of the muscles, dependent perhaps on defective nutrition*', although there remained '*confusion with progressive neural muscular atrophy*'. The solution to Meryon's acknowledged uncertainty was resolved in France, by Duchenne, whose work was based on careful clinical studies, together with his innovative 'muscle harpoon' muscle biopsy technique, that enabled study of muscle tissue at various stages in the disease, leading to his major publication of 1868.<sup>1</sup> However, Gowers notes that Duchenne did not have opportunity to examine the nervous system at autopsy until 1871 when he confirmed the absence of pathological changes.

Emery and Emery<sup>7</sup> have suggested that Meryon's contribution to understanding of pseudohypertrophic muscular dystrophy has been largely neglected. While it is true that his work has not featured in modern publications and the common eponym belongs to Duchenne, his early work has been properly recognised, for example by Gowers in his highly influential *Manual*<sup>2</sup>, by German researchers, such as Friedreich, and in the 20th century by Walton and Nattrass<sup>6</sup>, and by Adams, Denny-Brown and Pearson<sup>8</sup>. Meryon's publications appeared in the 19th century era of clinical description, at a time when

neuropathological studies were very much in their infancy, and before the advent of muscle biopsy. The rapid accumulation of new syndromic descriptions is a feature of contemporary major textbooks, notably by those of Gowers, Kinnier Wilson, Oppenheim and Brain; no progress could be made until these important clinical issues were resolved by consensus, a process that was set in train for muscle diseases by Walton and Nattrass<sup>6</sup>, who acknowledged Meryon in the first paragraph of their long paper in *Brain*. Meryon's contribution, therefore, was not neglected but was simply absorbed into the corpus of contemporary knowledge.

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## Meryon and the French Literature

Jacqueline Mikol and Olivier Walusinski, Paris, Email: [jacqueline.mikol@wanadoo.fr](mailto:jacqueline.mikol@wanadoo.fr); [walusinski@baillement.com](mailto:walusinski@baillement.com)

In 1852, **Edward Meryon (1809–1880)** reported a familial disease entitled “*On granular and fatty degeneration of the voluntary muscles*”, in which lesions were strictly limited to muscles, the central nervous system being preserved. As Meryon knew the French literature (Cruveilhier 1848, 1853; Aran 1850), he proposed the appellation of “*progressive muscular atrophy*”. This was the beginning of a quarrel because a neural process was subsequently demonstrated in progressive muscular atrophies.

**Guillaume Duchenne de Boulogne (1806–1875)**, who had described a pseudo-hypertrophic muscular paralysis in a young boy (only published in 1868), denied the similarities of the cases and criticized the histological data. Subsequently, when Meryon claimed before the Royal Society (1867), the priority of the discovery of a purely myogenic disease, Duchenne was

vehemently opposed (1868). “*The honor of this discovery totally belongs to France*”. It is only in 1872 that Duchenne recognized that “*the patient described by E. Meryon is certainly affected by the disease that I have described in 1866 under the name of pseudo-hypertrophic paralysis or myosclerotic paralysis*” (1872). (See Delaporte and Pinell for a detailed report.)

**Charles Spielmann (1834–1863)** described in 1862 the clinical findings in a young boy and discussed at length earlier reports, briefly mentioning the autopsy report by Meryon.

At the same period, other physicians argued for and against Meryon.

Among those against Meryon:

**In 1853, Henri-Sauveur-Victor Bouvier (1799–1879)** maintained that the modifications of muscles were “*identical to the modifications described in the Mémoire of Cruveilhier*”, and that the disease was the consequence of a paralysis.

According to **Georges Hayem (1841–1933)**

- The notion of a primary involvement of muscle was not accepted (1869).
- Although the nervous system was totally normal, “the disease had to be considered as due to a lesion of the nervous system” (1876).
- The work of Meryon was considered as nonsignificant (1879).

According to **Achille Kelsch (1841–1911)**, Meryon “*made an error in what he had observed*” (1876).

Among those in favor of Meryon

- **Eugene Bouchut (1818–1891)**, who studied a necropsy case, confirmed that “*it is the muscle disease which induces the paralysis*” (1867). This observation was criticized by Duchenne (1872).
- **Jean-Martin Charcot (1825–1893)** described the first French necropsy from a case of pseudo-hypertrophic paralysis which was then unanimously recognized (1871).
- **Jean-Baptiste Vincenz Laborde (1830–1903)** concluded “*Whatever has happened and whatever the work carried out by Mr. Duchenne, Meryon's results will remain the first according to nosology in impartial history of Science*” (1871).

To forget the quarrel about the name of the disease let us remember that the disease has now a large genetic basis, recognized as dystrophinopathies.

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### Awareness of Meryon's Work in the German Medical Literature

*Hans H. Goebel, Consultant in Myopathology, Institute of Neuropathology, Charité, Berlin/Germany. Email: [hans-hilmar.goebel@charite.de](mailto:hans-hilmar.goebel@charite.de)*

As for historical reviews of times before the last century only printed material (texts and images) is available, papers, textbooks, doctoral dissertations and, especially in Germany, theses for habilitation are the basis to assess awareness and impact of Edward Meryon's work among German clinicians. Here, only few selected publications and their contents can be cited, which, however, may not represent the complete picture.

Just three years after Meryon's publication (1852), Zacharias Oppenheimer submitted his "Habilitationsschrift" to the

Heidelberg Medical Faculty on "Progressive fatty Degeneration of the Muscle" in which he mentioned Meryon as describing the inheritance of the disease in males and quoting in the original his finding normal spinal cord and peripheral nerves in his patients at autopsy.

Friedberg, in 1858, in his monograph "Pathology and Therapy of Muscle Paresis" writes extensively on Meryon's work quoting his English original text as well as commenting it. C. Sigmundt (1867) refers to Meryon's description of four brothers in his paper. Friedreich (1873) in his book "On Progressive Muscular Atrophy, on true and Spurious Muscle Hypertrophy" notes that "Meryon, to our knowledge, provided first evidence of the histopathology and deemed fatty degeneration of myofibers an essential process". This statement of a leading German neurologist at his time not only documents knowledge of Meryon's work, but also sets the record of the first description right, early in the contest. In the "Handbook of Neurology", edited by Lewandowsky (1911) Meryon is mentioned as having described a family and found the central nervous system intact, but no reference of Meryon's work is given, perhaps, because today's rigid criteria of complete citations were not applied in 1911.

However, there were many German authors describing what is now considered Duchenne muscular dystrophy (DMD) who omitted Meryon from their reports.

Emery and Emery (2011) quote a list (p.84) of patients in the German literature reviewed by Duchenne of whom, however, the first, Spielmann, wrote in French from Strasbourg in 1862 when Strasbourg was French and not German which it became in 1871. Duchenne/Emery list 14 German patients one of whom extensively described by Griesinger (1865) examining biopsied rather than autopsied muscle tissue, some with DMD in a familial fashion, of whom only one author, Heller (1866) refers indirectly to Meryon quoting Friedberg's book. It appears that knowledge and information on Meryon's work faded over the years, in particular when not cited in the publications of prominent German myologists, such as Erb, and disappeared from textbooks and papers. Even in the chapter "Dystrophy – historical Part" in the Handbook "Congenital early Acquired Heredofamilial Disorders" by Hans Curschmann whose name is connected to myotonic dystrophy (DM1) as Curschmann–Steinert disease in German medicine, Meryon is not mentioned "Erb's dystrophy – Dystrophia Musculorum Progressiva, a generic term (HHG) – first exactly described by Duchenne, but earlier by Semmola, Coste & Gioja, Leyden, Griesinger, Eulenburg, Seidel, and others".

Only recently, prompted by Emery and Emery's first edition (1995) of their book, C. Mainberger in his doctoral thesis from Würzburg (2004) gives credit to Meryon's work: "The first systematic clinico-pathological study on the Duchenne type is by E.Meryon". Thus, awareness of Meryon's work has reappeared in the German literature and will spread as the custom to distribute copies of German dissertations to all German speaking universities was still in place at that time – today replaced by electronic availability.

Comparing the respective French literature with the German one, it is obvious that the Germans only quoted Meryon's work, but did not criticize it while the French interpreted Meryon's work.

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